

REMARKS

Reconsideration and allowance are respectfully requested.

Claims 19 and 21-30 are now pending, with Claim 19 being the sole independent claim.

Turning now to the Office Action mailed December 30, 2003:

Regarding the question about the Sequence Listing and the region of SEQ ID NO:9 that encodes SEQ ID NO:10, the total length of the isolated cDNA consists of 3936 bp (SEQ ID NO:9) and is believed to contain a single open reading frame of 3261 bp (from 144-3404) encoding a functionally complete protein of 1086 amino acids (SEQ ID NO:10). Applicants note that there is an ATG codon at position 144-146 and the termination codon is at position 3402-3404 (TAG). The start methionine in SEQ ID NO:10 can be found at position 1.

Regarding the Drawings, Applicants request entry of the attached Replacement Drawing Sheets (described above). The specification has been amended to refer to the new view numbering of the figures. No new matter has been added.

Regarding the Section 112, first paragraph written description rejection, Applicants respectfully traverse.

Under the PTO Written Description Guidelines, the written description requirement is met with disclosure of "functional characteristics when coupled with a known or disclosed correlation between function and structure." Guidelines, 66 Fed. Reg. at 1099.

Applicants submit that there is a well-known correlation between the cellulose synthase activity disclosed and claimed in the instant specification and cellulose synthase protein (and corresponding nucleic acid) structure.

Applicants believe the following references to be representative of the knowledge of one of ordinary skill in the art:

Delmer (*Ann. Rev. Plant Physiol. Plant Mol. Biol.* 50:245-276 (1999)) ("Delmer")
Holland et al. (*Plant Physiol.* 123:1313-1323 (2000)) ("Holland")
Richmond et al. (*Plant Physiol.* 124:495-498 (2000)) ("Richmond et al.")
Richmond (*Genome Biology* 1(4):reviews3001.1-3001.6 (2000)) ("Richmond")

Each of these references, except Richmond et al. which was cited in the originally-filed IDS, are cited in a Supplemental IDS filed simultaneously herewith.

Cellulose synthases described to date have a number conserved structural features:

1. At the amino terminus of the protein is an amino acid domain that bears some resemblance to a zinc finger or LIM transcription factor. See, e.g., Richmond et al., page 496, column 1.
2. Within this zinc finger domain is a strictly conserved sequence motif, known as the 'CXXC' motif. This motif has the following single-letter amino-acid code, where X is any amino acid:

CX₂CX₁₂FXACX₂CX₂PXCX₂CXX₅GX₃CX₂C

See, e.g., Richmond, page 2, column 1.

3. There are three conserved aspartic acid (D) residues that are widely spaced (a single D, followed by a DXD, and then a third D). See, e.g., Delmer, page 258, Figure 2; and Richmond, page 2, column 2]
4. Following the third aspartic acid is another conserved motif (QXXRW) that is thought to form the active site together with the three aspartic acid residues. See, e.g., Delmer, page 258, Figure 2; and Richmond et al., page 496, column 2.
5. There are eight putative transmembrane helices – two in the amino terminus and six in the carboxy terminus. See, e.g., Delmer, page 266, Figure 3; and Holland, page 1313, column 2.

Appendix A, attached hereto, is a Clustal V alignment of SEQ ID NO:10 of the instant claims and GI 2827141 (*Arabidopsis thaliana* cellulose synthase cited in the instant application).

The above 1-4 conserved structural features for these two sequences are identified in Appendix A by boxes and labels.

Furthermore, regarding the above-described fifth conserved structural feature, PSORT (www.psорт.nibb.ac.jp; PSORT program was coded by: Kenta Nakai, Ph.D., Human Genome Center, Institute for Medical Science, University of Tokyo, Japan (knakai@ims.u-tokyo.ac.jp)) was used with the instant SEQ ID NO:10 to assign putative transmembrane domains.¹ The following output illustrates eight putative transmembrane helices – two in the amino terminus and six in the carboxy terminus:

ALOM program	count: 8	value: -8.12	threshold: 0.5
INTEGRAL	Likelihood = -8.12	Transmembrane	1059 - 1075 (1056 - 1079)
INTEGRAL	Likelihood = -4.57	Transmembrane	909 - 925 (904 - 928)
INTEGRAL	Likelihood = -4.09	Transmembrane	301 - 317 (300 - 322)
INTEGRAL	Likelihood = -4.09	Transmembrane	1002 - 1018 (994 - 1019)
INTEGRAL	Likelihood = -3.08	Transmembrane	278 - 294 (274 - 295)
INTEGRAL	Likelihood = -2.97	Transmembrane	880 - 896 (878 - 897)
INTEGRAL	Likelihood = -0.27	Transmembrane	1034 - 1050 (1034 - 1050)
INTEGRAL	Likelihood = 0.26	Transmembrane	945 - 961 (945 - 961)

Given this known correlation between cellulose synthase activity and protein structure, Applicants submit that one of ordinary skill would readily recognize where amino acid substitutions could be made to result in a polypeptide sequence having 85% sequence identity to SEQ ID NO:10 while still retaining cellulose synthase activity.

Thus, the combination of the Applicants' disclosure and the known correlation of function and amino acid sequence structure renders the claims in compliance with the written description requirement.

Withdrawal of the Section 112, first paragraph written description rejection is respectfully requested.

Regarding the Section 112, first paragraph enablement rejection, Applicants respectfully traverse.

Applicants submit that the specification enables a person of ordinary skill to make and use the claimed invention commensurate in scope with the pending claims.

The above remarks in response to the Section 112, first paragraph written description rejections are also applicable here.

As discussed *supra*, the specification coupled with the extensive knowledge about conserved residues present in the art provides specific guidance to one of

¹ PSORT employs Klein et al. method ("ALOM", also called as KKD) to detect potential transmembrane segments (P. Klein, M. Kanehisa, and C. DeLisi, *Biochim. Biophys. Acta*, 815:468 (1985)). It attempts to identify the most probable transmembrane segment from the average hydrophobicity value of 17-residue segments, if any. It predicts whether the segment is a transmembrane segment (INTEGRAL) or not (PERIPHERAL) comparing the discriminant score (reported as 'value') with a threshold parameter pre-defined to 0.0 for bacteria ('threshold'). For an integral membrane protein, position(s) of transmembrane segment(s) are also reported. Their length is fixed to 17 but their extension, i.e., the maximal range that satisfies the discriminant criterion, is also given in parentheses. The discrimination step mentioned above is continued after leaving out the segment till there remains no predicted transmembrane segment. The item 'count' is the number of predicted transmembrane segments.

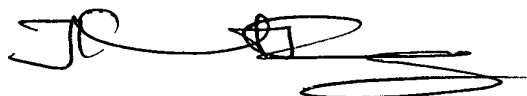
ordinary skill as to which structures are likely to have enzyme activity. Furthermore, the experimentation necessary to determine activity is not undue in this field, where the level of skill is very high. Applicants disclose methods for expressing the recombinant constructs in monocot, dicot and microbial cells (see prophetic Examples 4-6 of the instant specification). With the expressed polypeptide, activity may be determined using routine tests. Applicants submit that one of ordinary skill in the art could carry out these methods without undue experimentation.

In view of the foregoing, Applicants respectfully request withdrawal of the Section 112, first paragraph enablement rejection.

Applicants believe the foregoing to be responsive to each of the points raised in the Office Action. Allowance of the above-referenced application is respectfully requested.

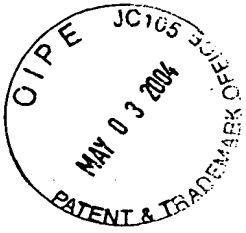
If applicable, please charge any fees or credit any overpayment of fees which are required in connection herewith to Deposit Account No. 04-1928 (E. I. du Pont de Nemours and Company).

Respectfully submitted,

A handwritten signature in black ink, appearing to read 'J. KENNETH JOUNG', with a stylized flourish extending to the right.

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Dated: 30 April 2004



Appendix A

#1 and #2 - zinc finger resembling LIM and 'CXXC' motif

1	M.....L.AGSHNRNE.V.I..D.....E..GQ.CQICGD...L.....FVACNE	Consensus #1	BB1170USPCTSeqIdNo10
1	10 20 30 40 50 60		GI 2827141
	MEASAGLVAGSHNRNELVVIR/DGDPGPKPPEEQNGOV/CQICGDDVGLAPGGDPFVACNE		
	MNTGGRLLIAGSHNRNEFVLINAD/SARIRSVQELSGQT/CQICGDEIELTVSSELEFVACNE		
61	CAFPVCR.CYEYERREG.Q.CPOCKTRYKR.KG..RV.GD.EEE...DDL..EF...G.D	Consensus #1	BB1170USPCTSeqIdNo10
61	70 80 90 100 110 120		GI 2827141
	CAFPVCRDCYEYERREGTONCPQCKTRYKRLKGCQRTGCD-EEEDGVDDLDNEFNWDGHD		
	CAFPVCRPCYEYERREGNCA/CPOCKTRYKRIKGSPPVDEDD/EEEDIDBLEYEFD-HGMD		
AE..L.....GRGG.....P.....PLLT.....D.....HAL.....G	Consensus #1	
120	130 140 150 160 170 180		
120	SQSVAESMLYGHMSYGRGGDPNGAPQAFQLNENVPLLTNGQMVDDIPPEQHALVPSFMGG	Consensus #1	BB1170USPCTSeqIdNo10
	PEHAEAAALSSRLNTGRGGLDAPP- ----GSQIPLLLTYCDEDA/DMYSDRHALIVPPSTG	GI 2827141	
	.G.R..P.P..D.S.P.Q.RSM.P.KD.A.YGYGSVAWK.RME.WK.RQ...Q.....G	Consensus #1	
180.	190 200 210 220 230 240		
175	GGKRJHPLPYADPSLPVQPRSMDFPSKDLAAAYGYGSVAWKERMENWKQQRERMHQTGNDGG	Consensus #1	BB1170USPCTSeqIdNo10
	YGNRVYPAPFTDSAPPQARSMPQKDI/AEYGYGSVAWKDRMEVWKRRQGEKLVIKHEG	GI 2827141	
	G...G.....DD.D.P.MDE.RQ.LSRK.P..SS.INPYRM.I..RL..LG.FFHYR	Consensus #1	
240	250 260 270 280 290 300		
235	GDDG- ----DDADLPLMDEARQQLSRKILPLPSSQINPYRMIIIRLVVLGFFFFHYR	Consensus #1	BB1170USPCTSeqIdNo10
	GNNGRGSDDDDELDDPDMPMMD/EGROPLSRKLEIRSSRINPYRMLILCLRLLAILGLLEFFHYR	GI 2827141	

Appendix A

291	..HPVNDA..LWL.SVICEIWEA.SWILDQFPKW.PIERETYLDRLSLR..KEG.PS.LA	Consensus #1
295	310 320 330 340 350 360	
	V M H P V N D A F A L W L I S V I C E I W F A M S W I L D Q F P K W P I E R E T Y L D R L S L R F D K E G O P S Q L A	BB1170USPCTSeqIdNo10
	I L H P V N D A Y G E W L T S V I C E I W F A V S W I L D Q F P K W P I E R E T Y L D R L S L R Y E K E G K P S G L A	GI 2827141
	#3 - conserved D	
	P . D . F V S T V D P L K E P P L . T . N T V L S I L . V D Y P V D K V . C Y V S D D G A A M L T F E A L S . T . E F A	Consensus #1
	370 380 390 400 410 420	
351	P I D E F V S T V D P L K E P P L V T T N T V L S I L S V D Y P V D K V S C Y V S D D G A A M L T F E A L S E T S E F A	BB1170USPCTSeqIdNo10
355	P V D V E F V S T V D P L K E P P L I T A N T V L S I L A V D Y P V D K V A C Y V S D D G A A M L T F E A L S D T A E F A	GI 2827141
	#3 - conserved D	
	. K W V P E C K . . N I E P R A P E W Y F . Q K . D Y L K . K V . . F V R R E R R A M K R . Y E E F K V . I N A L V A .	Consensus #1
	430 440 450 460 470 480	
411	K W V P E C K R Y N I E P R A P E W Y F Q O K I D Y L K D K V A A N F V R E R R A M K R E Y E E F K V R I N A L V A K	BB1170USPCTSeqIdNo10
415	R K W V P E C K K F N I E P R A P E W Y F S Q K M D Y L K N K V H P A F V R E R R A M K R D Y E E F K V K I N A L V A T	GI 2827141
	#3 - conserved D	
	A Q K V P E E G W T M Q D G T P W P G N N V R D H P G M I Q V F L G . S G . . D . . G N E L P R L V Y V S R E K R P G .	Consensus #1
	490 500 510 520 530 540	
471	A Q K V P E E G W T M Q D G T P W P G N N V R D H P G M I Q V F L G S G G L D C E G N E L P R L V Y V S R E K R P G Y	BB1170USPCTSeqIdNo10
475	A Q K V P E E G W T M Q D G T P W P G N N V R D H P G M I Q V F L G H S G V R D T D G N E L P R L V Y V S R E K R P G F	GI 2827141
	#3 - conserved D	
	. H H K K A G A M N . L . R V S A V L . N A P Y L L N . D C D H Y I N N S K A I . E . M C F M M D P . . G K K V C Y V Q	Consensus #1
	550 560 570 580 590 600	
531	N H H K K A G A M N A L V R V S A V L T N A P Y L L N I D C D H Y I N N S K A I K E A M C F M M D P L L G K K V C Y V Q	BB1170USPCTSeqIdNo10
535	D H H K K A G A M N S I R V S A V L S N A P Y L L N V D C D H Y I N N S K A I R E S M C F M M D P Q S G K K V C Y V Q	GI 2827141
	#3 - conserved D	

Appendix A

	FPQRFDGIDRHDY.NRNVVFFEDINMKGLDGIQGPIYVGTGCVFRRQALY.G.DAPK.KKP	Consensus #1
591	610 620 630 640 650 660	
595	EPQRFDGIDRHDYANRNVVFFEDINMKGLDGIQGPIYVGTGCVFRRQALYGYDAPKTKKP	BB1170USPCTSeqIdNo10
	EPQRFDGIDRHDYSNRNVVFFEDINMKGLDGIQGPIYVGTGCVFRRQALYGFDA PKKKKP	GI 2827141
	P..TCNCWPKWC.C.CC.G.RK..KT.K.K.K.....E.....AL...DE....	Consensus #1
	670 680 690 700 710 720	
651	PSRTGNCWPKWCFCGCCGFGNRKQKTTKPKTEKKKLLFEKKEENQSPAYALGEIDEAA--	BB1170USPCTSeqIdNo10
655	PGKFCNCWPKWC-CLCG-GLRKKSKT-KAKDKTN-----TKETSKQIHAIENVDGVIV	GI 2827141
	P....EK.....Q.KLEKKFGQS.VFV.S..L.NGG....ASPA.LL.EAI.VISCGYED	Consensus #1
	730 740 750 760 770 780	
709	PGAENEKAGIVNQKLEKKFGQSSVFVTSILLENGGLKSPASLLKEA-HVISCGYED	BB1170USPCTSeqIdNo10
707	PVSNVEKRSEATQLKLEKKFGQSPVEVASAVLQNGGVPRNASPACLLREAIQVISCGYED	GI 2827141
	KT.WGKEIGWIYGSVTEDILLTGFKMHCHGWS.YC.PKR.AFKGSAP.NLSDRLHQVLRW	Consensus #1
	790 800 810 820 830 840	
769	KTDMGKEIGWIYGSVTEDILLTGFKMHCHGWSIYCI PKRVAFKGSAPLNLSDRLHQVLRW	#4 - conserved QXXRW
767	KTEWGKEIGWIYGSVTEDILLTGFKMHCHGWSVYCM PKRAAEFKGSAPINLSDRLHQVLRW	BB1170USPCTSeqIdNo10
	ALGS.EIF.S.HCP.WYGYGGGLK.LERFSYINS.VYPWTS.PL..YC.LPA.CLLTGKF	GI 2827141
	850 860 870 880 890 900	
829	ALGSIEIFFSNHCP.LWYGYGGGLKFLERFSYINSIVYPWTSIPLLAYCTLPACLLTGKF	BB1170USPCTSeqIdNo10
827	ALGSVEIFLSRHCP.LWYGYGGGLKWLERFSYINSIVYPWTSPLIVYCSLPACLLTGKF	GI 2827141

Appendix A

	I . P E . . . N . A F M . . . F I . I . . . T . I L E M . W . G V G I D D W W R N E Q F W V I G G . S S H L F A . F Q G	Consensus #1
889	I T P E L N N V A S L W E M S L P I C I F A T S I L E M R W S G V G I D D W W R N E Q F W V I G G V S S H L F A V F Q G	BB1170USPCTSeqIdNo10
887	I V P E I S N Y A G I L E M L M F I S L A V P G I L E M Q M G V G I D D W W R N E Q F W V I G G A S S H L F A L F Q G	GI 2827141
	L L K V . A G V . T . F T V T S K . . D D . . F S E L Y . F K W T T L L I P P T T L L . . N . I G V . . G V S . . A I . N	Consensus #1
949	L L K V I A G V D T S E T V T S K G G D D E E F S E L Y T F K W T I L L I P P T T L L L N F I G V V A G V S N A I N N	BB1170USPCTSeqIdNo10
947	L I K V L A G V N F N E T V T S K A A D D G A F S E L Y I F K W T T L L I P P T T L L I I N I I G V I V G V S D A I S N	GI 2827141
	G Y . S W G P L F G . L F F A . W V I V H L Y P F L K G . . G . Q . . . P T I . . V S I L L A S I . . L L W V R . . P	Consensus #1
1009	G Y E S W G P L F G K L E T F A F W V I V H L . P F L K G L V G R K N R T P T I V I V S I L L A S I F S L L W V R I D E	BB1170USPCTSeqIdNo10
1007	G Y D E S W G P L F G R I F F A L W V I V H L . P F L K G M L E K Q D K M P T I I V V S I L L A S I L T L L W V R V N P	GI 2827141
	F . A K . . G P . L E . C G L . C . .	Consensus #1
1069	F L A K D D G P L L E E C G L D C N .	BB1170USPCTSeqIdNo10
1067	F V A K G - G P V L E I C G L N C G N	GI 2827141

Consensus #1: When all match the residue of BB1170USPCTSeqIdNo10 show the residue of BB1170USPCTSeqIdNo10, otherwise show ‘.’

Shade (with black at 40% fill) residues that match BB1170UPCTSeqIdNo10 exactly.